

# Risk factors for syphilis infection among pregnant women: results of a case-control study in Shenzhen, China

Hua Zhou, Xiang-Sheng Chen, Fu-Chang Hong, Peng Pan, Fan Yang, Yu-Mao Cai, Yue-Ping Yin, Rosanna W Peeling, David Mabey

*Sex Transm Infect* 2007;**83**:476–480. doi: 10.1136/sti.2007.026187

**Background:** China has been experiencing a rapidly growing syphilis epidemic since the early 1990s, with the reported incidence of congenital syphilis increasing from 0.01 cases per 100 000 live births in 1991 to 19.7 cases per 100 000 live births in 2005. Detailed studies of risk factors for syphilis in pregnant women are needed to inform new preventive interventions.

**Objective:** To investigate factors associated with recent syphilis infection among pregnant women and recommend strategies for improved preventive interventions in the community.

**Methods:** A case-control study was conducted among women attending antenatal clinics in Shenzhen City, South China. Cases were antenatal clinic women testing positive for early syphilis, based on laboratory results, with those testing negative being controls. All participants completed the same anonymous questionnaire covering demographics, lifestyle, sexual behaviour, and sexual partnerships.

**Results:** 129 cases and 345 controls were recruited. Syphilis was significantly associated with unmarried status, less education, multiple sex partners, travel of sex partner in the past 12 months, a history of induced abortion, and previous sexually transmitted infections. Overall, there were no differences between syphilis-positive and negative women in household registration status (*hukou*), living district and duration in Shenzhen, monthly income, and age at first sex.

**Conclusions:** Many demographic and behavioural risk factors are associated with syphilis among pregnant women. In the government congenital syphilis control programme, comprehensive preventive interventions should be provided in all clinical settings in addition to the current procedures for syphilis screening among antenatal women.

See end of article for authors' affiliations

Correspondence to: Dr Xiang-Sheng Chen, National Center for STD Control, 12 Jiangwangmiao Street, Nanjing 210042, China; chenxs@vip.163.com

Accepted 8 July 2007

China is suffering a mounting epidemic of syphilis. Data from the China national information system for disease control and prevention have indicated that the reported incidence of primary and secondary syphilis has increased in recent years to 7.63 cases per 100 000 individuals in 2006,<sup>1</sup> although the system did not improve significantly. The rate of congenital syphilis has increased even more dramatically, with an average yearly rise of 71.9%, from 0.01 cases per 100 000 live births in 1991 to 19.68 cases per 100 000 live births in 2005, consistent with a generalized epidemic.<sup>2</sup> A comprehensive review of syphilis rates among pregnant women (usually considered as a proxy of the general population) in China has revealed an increasing seroprevalence of the infection, with a median prevalence of 0.45%.<sup>3</sup> Shenzhen, a "special economic zone" located in south coastal China and adjacent to Hong Kong, has witnessed an alarmingly rapid spread of sexually transmitted infections (STIs) in recent years; in particular, the syphilis incidence rate increased from 1.4 per 100 000 individuals in 1984 to 36.6 in 2003. In women, there has been an almost 40-fold increase in the past 20 years, from 1.2 to 43.8 per 100 000 individuals per year.<sup>4</sup> The local health bureau began offering free screening for syphilis and HIV in pregnant women as part of a comprehensive syphilis control programme in July 2001.<sup>5</sup> The health bureau's target is to decrease rates of congenital syphilis from 65 per 100 000 live births in 2001 to less than 25 per 100 000 live births by 2008. To identify the risk factors for syphilis to enable local authorities to develop an evidence-based syphilis control programme, we undertook a case-control study of sociodemographic and behavioural risk factors associated with syphilis among antenatal clinic attendees in the city.

## METHODS

Participants were recruited from the local antenatal clinics in five of the six administrative districts of Shenzhen City between March and November 2005. The population in these five districts accounts for more than 95% of the total population. Eligible participants were women attending antenatal clinics for prenatal care, aged 18 years or over, and able to give informed consent. All clinic attenders were informed of the study. Blood for syphilis serology was drawn as part of the clinic routine. Potential study participants were identified through screening with a rapid syphilis test (SD Bioline syphilis 3.0; Standard Diagnostics, Inc., Korea). Study participants seropositive for the rapid test were identified as "cases" at the time of screening. For each "case", the next three individuals seronegative for the rapid test were selected as "controls". After obtaining informed consent, "cases" and "controls" were asked to complete a questionnaire with the help of a trained interviewer. Screening with rapid plasma reagin (RPR; Shanghai Rongsheng Biotech Co. Ltd., Shanghai, China) and confirmation with *Treponema pallidum* particle agglutination assay (TPPA; Serodia-TP, Fujirebio Inc., Tokyo, Japan) was finally used to categorise the cases (i.e. those with positive RPR and TPPA tests) and controls (i.e. those with negative RPR). There was excellent agreement (100%) between SD Bioline and TPPA. Our intention was to enroll cases and controls in a 1 : 3 ratio from the same source clinic but, overall, slightly more cases were recruited (129 cases and 345 controls). Laboratory results (RPR and TPPA) were used for treatment according to

**Abbreviations:** RPR, Rapid plasma reagin; STI, sexually transmitted infection; TPPA, *Treponema pallidum* particle agglutination assay

current treatment guidelines.<sup>6</sup> The study was approved by the World Health Organisation Research Ethics Review Committee and the Medical Ethics Committee of the National Center for Sexually Transmitted Disease Control in Nanjing.

Data from questionnaires and laboratory tests were double-entered using EpiData software (EpiData Association, Denmark). A univariate comparison of variables between cases and controls was undertaken. Crude odds ratios (OR) are given with corresponding 95% confidence intervals (CI). Variables that were significant at  $p < 0.10$  in univariate analyses were selected for multivariate logistic analysis. Multivariate model variables with a probability level of  $p \leq 0.05$  were considered statistically significant. SPSS for Windows 11.0 (SPSS Inc., Chicago, Illinois, USA) was used to analyse the data.

## RESULTS

A total of 474 women participated in the study, of which more than half (55.4%) were from two administrative districts, namely Longgang and Baoan Districts. Their mean age was  $27.5 \pm 4.1$  (standard deviation, SD) for cases and  $27.0 \pm 3.8$  (SD) for controls. Most subjects (87.1%) had migrated from other areas without the possession of a Shenzhen household registration card (*hukou*).

A comparison of sociodemographic, medical and behavioural characteristics using univariate analysis showed that cases were more likely to be unmarried, to have lower educational attainment, to be self-employed or unemployed, and to have a lower monthly income. They were significantly more likely to report a previous STI, histories of spontaneous or induced abortion, earlier age at first sex, multiple sexual partners, and a sexual partner who had overnight travel in the past 12 months (table 1).

In multivariate logistic analysis (table 2), risk factors significantly associated with syphilis were unmarried status (OR 4.48; 95% CI 1.43–14.02), lower education (OR 8.61; 95% CI 2.18–34.04 for secondary school or less and OR 4.89; 95% CI 1.28–18.69 for high school or less compared with college or above level), having history of spontaneous (OR 3.23; 95% CI 1.31–7.99) or induced (OR 6.57; 95% CI 3.08–13.99) abortion, having a previous STI (OR 15.64; 95% CI 3.58–68.33), and having a sexual partner who had overnight travel during the past 12 months (OR 4.83; 95% CI 2.41–9.67).

Overall, approximately half (44.5%) of all participants reported having at least two sexual partners during their lifetime (68.5% of cases and 34.5% of controls,  $p < 0.001$ ), and one in five participants reported having first sex before 20 years of age, although this risk factor was not significant enough to remain at the final multivariate model. There were no significant differences between cases and controls in age, occupation, residence status (such as local *hukou*, living district and duration), and monthly income.

## DISCUSSION

To our knowledge, this is the first case-control study of risk factors for syphilis among pregnant women in China. Our study confirms that STI-related risk behaviours are substantial in pregnant women in the study area. Social forces are transforming the scope and dangers of sex in China. A nationwide population-based survey showed that 10% of men and 4% of women reported having sex with two or more non-commercial sexual partners in the past year.<sup>7</sup> In our study population, however, more than one-third reported having two or more sexual partners during their lifetime. The difference could be explained by the important characteristics of this population in which the majority were migrants or temporary residents. It is well known that the migration of historic proportions<sup>8</sup> has increased sexual risk among a subgroup of rural to urban

migrants who may serve as a bridging population for STI and HIV transmission.<sup>9</sup> Several small studies have indicated an increased risk of STI among rural to urban migrants in China.<sup>10–13</sup>

The risk factors identified in the current study, unmarried status, and lower educational attainment, largely confirm the findings from the previous studies in the study area or in China.<sup>14–16</sup> This study is the first to find a significant association of syphilis infection in pregnant women with the overnight travel of a sex partner during the past year. A population-based study has revealed that 9% of Chinese men paid for sex in the past year and when having sex with a commercial sex worker they typically failed to use a condom.<sup>7</sup> The data further confirm the worries regarding the bridging effects of the clients of commercial sex workers between the core group (high-risk population) and general populations.

A history of induced abortion was found to be associated with syphilis in our study. The association can be explained by the fact that an unwanted pregnancy is usually the result of unsafe sexual behaviour, which creates dual risks for both pregnancy and exposure to STIs. This has also been confirmed by previous studies in which high rates of STIs were observed among women seeking induced abortions in family planning clinics,<sup>17</sup> and in patients referred for termination of pregnancy.<sup>18</sup> Moreover, the high proportion (approximately 20%) in the case group reporting a previous STI suggests that an important opportunity to offer health promotion and behavioural intervention, aimed specifically at reducing future risk, may be being missed. It is urgent to encourage an integration of prevention interventions into clinical practice at settings such as STI clinics and family planning clinics, which currently seems not yet to be receiving adequate attention in the healthcare system in China.

A case-control study of risk factors for congenital syphilis in Shenzhen revealed a significant association of the disease in babies with the residence of their parents in Baoan and Longgang Districts.<sup>5</sup> Such an association was not, however, observed in our study for syphilis among pregnant women. This is probably related to a relatively poor intervention to prevent mother-to-child transmission of syphilis in these two districts, where more people are less educated than other districts, as shown in our study subjects (59.0% versus 32.1%,  $p < 0.001$ ), although residence area is not a risk factor for syphilis infection in pregnant women. Interestingly, our finding of an association between syphilis and the use of a condom in the most recent sex runs counter to our knowledge. The reasons are not well understood, although it may be that women using condoms have more sexual partners at high risk of infection or reflect an inconsistent condom use with casual partners.

Although the HIV problem in Shenzhen, southern Guangdong Province, is still much less serious than that in the southwest of China, it has been noted that sexual contact has been the major route of HIV transmission in the study area.<sup>19</sup> An increasing prevalence of syphilis and other STIs among pregnant women<sup>20–21</sup> could not only cause serious complications in this population, but also potentially fuel a heterosexual HIV epidemic in the future. Community-based intervention strategies to change sex-related risk behaviours among target high-risk (e.g. sex workers), bridge (e.g. bisexual men, clients of sex workers) as well as “low-risk” (sexually active women in monogamous relationships) populations are therefore urgently warranted, in addition to the current programme to implement syphilis screening in antenatal women in the study area. Guangdong Province has a resident population of over 91 million plus a floating population of more than 20 million, and ranks fourth in the reported incidence of syphilis (and third in congenital syphilis) among all provinces in mainland China. Therefore, the results of this study are

**Table 1** Univariate analysis: correlates of infection with syphilis among women attending antenatal clinics in Shenzhen, China

Variable	No. cases* (%)	No. controls* (%)	OR (95% CI)	P value
Current age (years)				
<25	32 (25.4)	107 (31.7)	1 (Referent)	
25–29	63 (50.0)	146 (43.2)	1.44 (0.88–2.36)	0.14
30+	31 (24.6)	85 (25.1)	1.22 (0.69–2.16)	0.50
Local residence				
Yes	13 (10.6)	45 (13.7)	1 (Referent)	
No	110 (89.4)	283 (86.3)	1.35 (0.70–2.59)	0.37
Living area				
Luohu District	26 (20.2)	69 (20.2)	1 (Referent)	
Futian District	20 (15.5)	35 (10.2)	1.52 (0.75–3.09)	0.25
Nanshan District	15 (11.6)	45 (13.2)	0.89 (0.42–1.85)	0.75
Longgang District	39 (30.2)	107 (31.3)	0.97 (0.54–1.73)	0.91
Baoan District	29 (22.5)	86 (25.1)	0.90 (0.48–1.66)	0.72
Duration of living in Shenzhen (year)				
<1	11 (9.7)	28 (9.9)	1 (Referent)	
≥1	102 (90.3)	254 (90.1)	1.02 (0.49–2.13)	0.95
Marital status				
Married	108 (83.7)	322 (94.2)	1 (Referent)	
Single or cohabiting	21 (16.3)	20 (5.8)	3.13 (1.63–6.00)	<0.001
Education				
Secondary school or below	76 (58.9)	145 (42.3)	3.55 (1.67–7.54)	0.001
High school	44 (34.1)	137 (39.9)	2.18 (1.00–4.74)	0.05
College or above	9 (7.0)	61 (17.8)	1 (Referent)	
Occupation				
Officer or professional	3 (2.3)	51 (14.9)	1 (Referent)	
Student	9 (7.0)	47 (13.7)	3.26 (0.83–12.75)	0.09
Factory worker	11 (8.5)	49 (14.3)	3.82 (1.00–14.51)	0.05
Self-employed	14 (10.9)	47 (13.7)	5.06 (1.37–18.74)	0.02
Jobless	76 (58.9)	129 (37.6)	10.02 (3.02–33.20)	<0.001
Other	16 (12.4)	20 (5.8)	13.60 (3.57–51.79)	<0.001
Income per month of participant (RMB yuan) <sup>†</sup>				
No income	54 (45.0)	81 (25.1)	4.00 (2.03–7.90)	<0.001
<1000	29 (24.2)	59 (18.3)	2.95 (1.41–6.16)	<0.01
1000–3000	24 (20.0)	105 (32.5)	1.37 (0.66–2.86)	0.40
>3000	13 (10.8)	78 (24.1)	1 (Referent)	
Age at first pregnancy (years)				
<20	22 (17.7)	14 (4.2)	7.18 (3.30–15.62)	<0.001
20–24	72 (58.1)	181 (54.5)	1.82 (1.12–2.94)	0.02
25 or above	30 (24.2)	137 (41.3)	1 (Referent)	
Time for first antenatal check				
1–12 Weeks of pregnancy	69 (54.8)	172 (52.6)	1 (Referent)	
13–26 Weeks of pregnancy	32 (25.4)	119 (36.4)	0.67 (0.42–1.08)	0.10
27 Weeks or later of pregnancy	25 (19.8)	36 (11.0)	1.73 (0.97–3.10)	0.06
Spontaneous abortion				
No	98 (81.7)	263 (88.3)	1 (Referent)	
Yes	22 (18.3)	35 (11.7)	1.69 (0.94–3.02)	0.08
Induced abortions				
No	26 (21.1)	155 (51.2)	1 (Referent)	
Yes	97 (78.9)	148 (28.4)	3.91 (2.40–6.37)	<0.001
Age at first sex (years)				
<20	44 (36.4)	43 (13.1)	7.67 (3.28–17.94)	<0.001
20–24	69 (57.0)	226 (68.7)	2.29 (1.04–5.02)	0.04
25 or above	8 (6.6)	60 (18.2)	1 (Referent)	
Number of lifetime sex partners				
1	35 (31.5)	173 (65.5)	1 (Referent)	
2 or more	76 (68.5)	91 (34.5)	4.13 (2.57–6.63)	<0.001
Condom use in most recent sex				
Yes	44 (36.4)	43 (13.1)	1 (Referent)	
No	69 (57.0)	226 (68.7)	0.52 (0.28–0.97)	0.04
Ever history of STI				
No	103 (81.1)	329 (98.5)	1 (Referent)	
Yes	24 (18.9)	5 (1.5)	15.33 (5.71–41.20)	<0.001
Income per month of sex partner (RMB yuan) <sup>†</sup>				
<1000	14 (11.5)	39 (12.0)	1 (Referent)	
1000–3000	56 (45.9)	147 (45.1)	1.06 (0.54–2.10)	0.87
>3000	52 (42.6)	140 (42.9)	1.04 (0.52–2.06)	0.92
Travel of sex partner in past 12 months				
No	71 (55.5)	272 (80.5)	1 (Referent)	
Yes	57 (44.5)	66 (19.5)	3.31 (2.13–5.14)	<0.001

CI, Confidence interval; OR, odds ratio; STI, sexually transmitted infection.

\*Totals may not sum to the recruited participants as a result of missing values.

<sup>†</sup>1 RMB yuan = US\$0.13 in 2006.

**Table 2** Multivariate analysis: correlates of infection with syphilis among women attending antenatal clinics in Shenzhen, China\*

Variable	No. cases (%)	No. controls (%)	OR (95% CI)	P value
Marital status				
Married	108 (83.7)	322 (94.2)	1 (Referent)	
Single or cohabiting	21 (16.3)	20 (5.8)	4.16 (1.38–12.54)	0.01
Education				
Secondary school or below	76 (58.9)	145 (42.3)	8.57 (2.30–31.91)	0.001
High school	44 (34.1)	137 (39.9)	3.98 (1.12–14.19)	0.03
College or above	9 (7.0)	61 (17.8)	1 (Referent)	0.001
No. of lifetime sex partners				
1	35 (31.5)	173 (65.5)	1 (Referent)	
2 or above	76 (68.5)	91 (34.5)	3.81 (1.94–7.49)	<0.001
Condom use in most recent sex				
Yes	44 (36.4)	43 (13.1)	1 (Referent)	
No	69 (57.0)	226 (68.7)	0.36 (0.14–0.94)	0.04
Ever history of STI				
No	103 (81.1)	329 (98.5)	1 (Referent)	
Yes	24 (18.9)	5 (1.5)	13.89 (3.49–55.29)	<0.001
Ever history of induced abortion				
No	26 (21.1)	155 (51.2)	1 (Referent)	
Yes	97 (78.9)	148 (48.8)	6.49 (3.03–13.91)	<0.001
Travel of sex partner in past 12 months				
No	71 (55.5)	272 (80.5)	1 (Referent)	
Yes	57 (44.5)	66 (19.5)	4.81 (2.43–9.55)	<0.001

CI, Confidence interval; OR, odds ratio; STI, sexually transmitted infection.

\*Totals may not sum to the recruited participants as a result of missing values.

worthy of some attention. The detection and treatment of syphilis represent important public health measures and are crucial to both HIV and congenital syphilis control and prevention. Currently, the Chinese government is developing a National Programme for Syphilis Control, one of the core components of which is increased awareness of syphilis prevention and enhanced screening among women attending antenatal care, and the consequent treatment of cases for prevention of mother-to-child transmission.<sup>22</sup>

Some limitations in the present study should be addressed. First, self-reported risk behaviours and STI histories may have been underreported during interviews, because some women may have been reluctant to divulge this information because of the conservative nature of Chinese culture regarding sex. Second, the participation bias in either case group or control group is another concern. In addition, missing data resulting from the inadequate skill of medical staff on questionnaire interview or the reluctance of interviewees to provide personal information may cause information bias. Furthermore, the sample size was generally small, although the coverage of administrative districts was good. Shenzhen has a population contributed to by the majority of provinces of China, but the sociodemographic and behavioural characteristics of its population are somewhat atypical among Chinese cities. Any generalisation of the results from this study should therefore be made with caution. A higher prevalence of syphilis among pregnant women has, however, been observed in the neighbouring province where the prevalence of syphilis in pregnant women was as high as 2.33%.<sup>23</sup>

In conclusion, many demographic and behavioural risk factors have been found to be associated with syphilis among pregnant women in the study area. These findings will be helpful for the government to direct and improve its comprehensive intervention programme on control of congenital syphilis.

## ACKNOWLEDGEMENTS

The authors are very grateful to clinic staff who recruited patients to this study. They would also like to thank all participants in this study for their cooperation in making the study possible. Special thanks to the Jiangsu Province's Key Medical Center of Dermatology and Venereology in Nanjing China.

## CONTRIBUTORS

XSC was principal investigator who was responsible for the study design, data analysis, and manuscript preparation. HZ and FCH were local principal investigators who were responsible for the local coordination of the study and inputs to manuscript preparation. PP, FY and YMC were responsible for field implementation and data management. YPY, RWP and DM were responsible for inputs and comments to the study design and manuscript preparation.

## Authors' affiliations

Hua Zhou, Fu-Chang Hong, Peng Pan, Fan Yang, Yu-Mao Cai, Institute of Dermatology, Shenzhen Chronic Disease Hospital, Shenzhen, China  
Xiang-Sheng Chen, Yue-Ping Yin, National Center for STD Control, Chinese Academy of Medical Sciences and Peking Union Medical College Institute of Dermatology, Nanjing, China  
Rosanna W Peeling, World Health Organization, Geneva, Switzerland  
David Mabey, London School of Hygiene and Tropical Medicine, London, UK

Funding: The study was supported by financial assistance from UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) (contract ID: OD/TS-05-00524).

Conflict of interest: None.

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